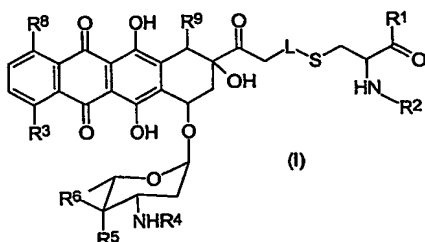


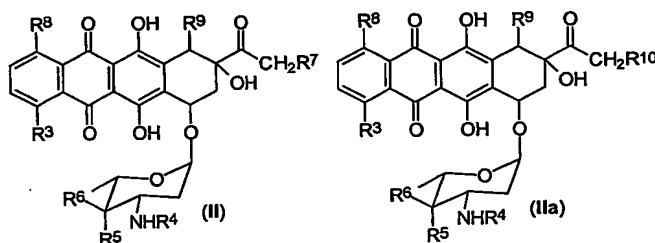
Claims

1. Method for the preparation of a compound of formula (I) or pharmaceutically acceptable salts thereof and intermediates thereof, comprising the steps of:



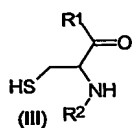
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- a) halogenating a compound of formula (II), resulting in compound of formula (IIa),



- b) reacting a compound of formula (IIa) at its 14 position with the thiol moiety of a peptide of formula (III), optionally in the presence of a suitable linker, to obtain said compound of formula (I),

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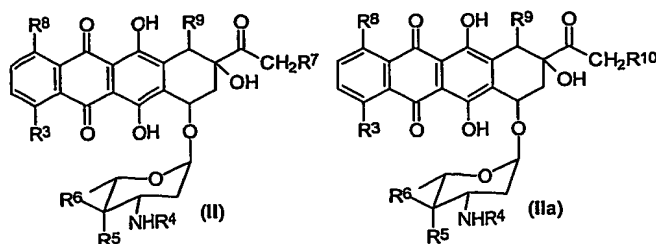


wherein R¹ represents OH, NH₂ or NH-peptide; R² represents H or -CO-peptide; R³ represents OCH₃, OH or H; R⁴ represents H, or COCF₃; R⁵ represents OH, O-tetrahydropyranyl or H; R⁶ represents OH or H; R⁷ represents H, OH, OCO(CH₂)₃CH₃ or OCOCH(OC₂H₅)₂; R⁸ represents OH or H; R⁹ represents OH or H; R¹⁰ represents a halogen and L is an optional suitable linker arm.

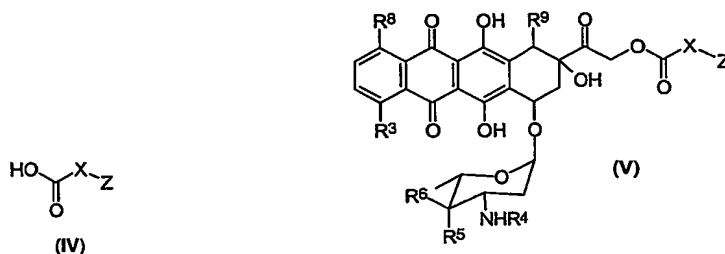
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2. Method according to claim 1, comprising the step of
 - a) halogenating the compound of formula (II), resulting in compound of formula (IIa),

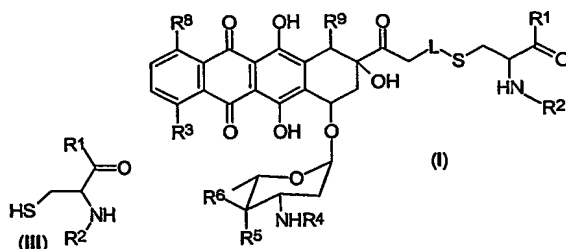
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b) reacting said compound of formula (IIa) at its 14 position with a linker of formula (IV) to obtain compound of formula (V), wherein Z is a functional group able to react with a thiol, and X represents a bivalent radical selected from the group comprising an alkyl, an aralkyl, an alkenyl, a cycloalkyl and an aryl radical



c) coupling said compound of formula (V) with the thiol moiety of a peptide of formula (III) to obtain compound of formula (I),

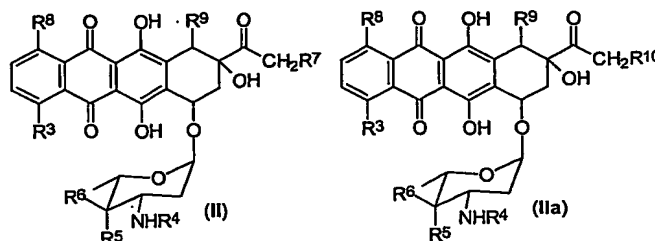


wherein L represents a linker arm of the formula $\text{R}-\text{X}-\text{Y}$ -, wherein R is $-\text{O}-\text{C}(=\text{O})-$, Y is the product of Z upon reaction with the thiol moiety of compound of formula (III) and X, R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^8 , R^9 and R^{10} have the same meaning as that defined above.

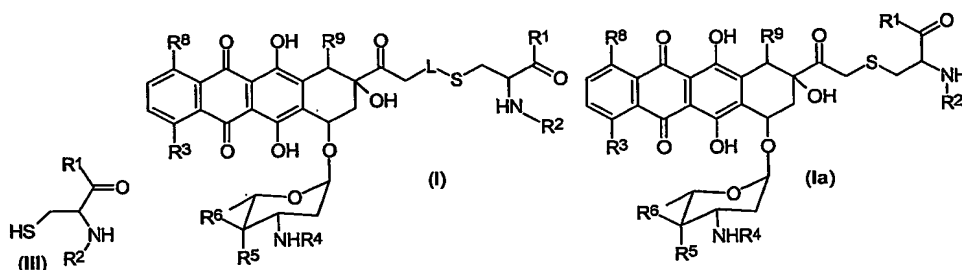
3. Method according to claim 1, comprising the step of

a) halogenating the compound of formula (II), resulting in compound of formula (IIa),

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b) reacting the compound of formula (IIa) at its 14 position with the thiol moiety of a peptide of formula (III) to obtain compound of formula (I)



5 wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^8 , R^9 and R^{10} have the same meaning as that defined above and $-L-$ is absent as represented by formula (Ia).

4. Method according to any of claims 1 to 3, wherein R^{10} is Br.

10 5. Method according to any of claims 1 to 4, wherein the halogenation step is done simultaneously with a ketalization step of the 13-ketone of the compound of formula (II) in the presence of a suitable alcohol.

15 6. Method according to claim 5, wherein the ketalization step is performed in the presence of a suitable orthoester.

7. Method according to claim 2, wherein the functional group Z is selected from the group comprising α,β -unsaturated carbonyl, carboxy, carbamoyl and imidyl radical.

20 8. Method according to claim 7, wherein the functional group Z is a maleimidyl radical.

9. Method according to claim 2, wherein said linker of formula (IV) is maleimidobutyric acid.

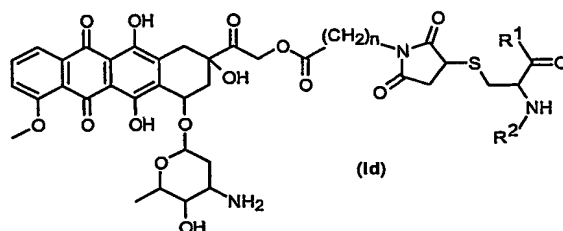
25 10. Method according to any of claims 1 to 9, wherein the compound of formula (II) is daunorubicin, carminomycin or idarubicin.

11. Method according to claim 10, wherein the compound of formula (II) is daunorubicin.

12. Method according to any of claims 1 to 11, wherein the peptide of formula (III) contains
5 from 1 to 100 amino acids.

13. Method according to claim 12, wherein the peptide of formula (III) contains from 10 to 30 amino acids.

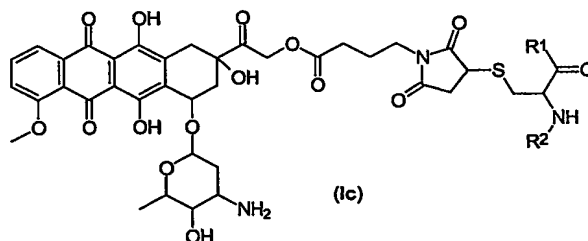
10 14. Method according to any of claims 1 to 2 and 4 to 13, wherein the compound of formula (I) is a compound of formula (Id)



wherein R^1 and R^2 have the same meaning as that defined above and n is a number ranging from 2 to 10.

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15. Method according to claim 14, wherein the compound of formula (Id) is a compound of formula (Ic)



wherein R^1 and R^2 have the same meaning as that defined above.

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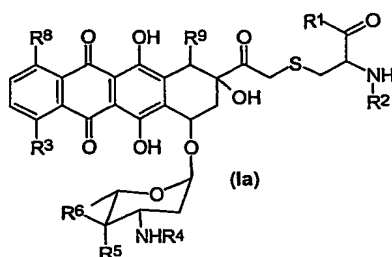
16. Intermediates obtained by the methods of claims 1 to 15.

17. Compounds obtained by the methods of claims 1 to 15.

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18. Compounds having the formula (Ia),

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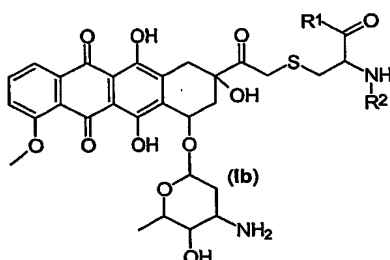


wherein R³ represents OCH₃, OH or H, R⁴ represents H or COCF₃, R⁵ represents OH, O-tetrahydropyranyl or H, R⁶ represents OH or H, R⁸ represents OH or H, R⁹ represents OH or H; R¹ represents OH, NH₂ or NH-peptide and R² represents H or –CO-peptide.

19. Compounds according to claim 18, wherein R³ represents OCH₃, OH or H, R⁴ represents H, R⁵ represents OH, O-tetrahydropyranyl or H, R⁶ represents OH or H, R⁸ is H, R⁹ is H; R¹ represents OH, NH₂ or NH-peptide and R² represents H or –CO-peptide.

20. Compounds according to claim 19, wherein R³ represents OCH₃, OH or H, R⁴ is H, R⁵ is OH, R⁶ is H, R⁸ is H, R⁹ is H; R¹ represents OH, NH₂ or NH-peptide and R² represents H or –CO-peptide.

21. Compounds according to claim 20, having the formula (Ib),



wherein R¹ and R² have the same meaning as that defined above.

22. Compound according to any of claims 17 to 21, wherein said compound contains from 1 to 100 amino acids.

23. Compound according to claim 22, wherein said compound contains from 10 to 30 amino acids.

24. Pharmaceutical composition comprising a pharmaceutical carrier and a therapeutically effective amount of a compound according to any of claims 17 to 23.

5 25. Compound according to any of claims 17 to 23, for use as a medicament.

26. Use of compound according to any of claims 17 to 23, as an antitumor agent.

10 27. Use of compound according to claim 16, as a precursor in the preparation of antitumor agent.

28. Use of compound according to any of claims 17 to 23, for the preparation of a medicament for the treatment of cancer.